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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,376	07/01/2003	John S. Patton	0005.15	3703

21968 7590 10/21/2004

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,376	PATTON ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims included in the prosecution are 1-25.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 20-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-18 of U.S. Patent No. 6,685,967. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claim in both patent and instant application are drawn to the same insulin powder composition with overlapping amount ranges (instant amounts are 5 to 99 % as opposed to 20 to 80 % in the patent). Instant specific size ranges for insulin particles, that is 'below 10 micrometers' are deemed to include 0.1 to 5 micrometer sizes in the patented claim 14in instant independent claim 20 which recites 'below 10 micrometers, which is generic with regard to the size ranges. Similar is the case with regard to patented claim (claim 14) which is generic with respect to the

pharmaceutical carrier and instant citrate in claim 26, trehalose in claim 49, mannitol in claim 55, raffinose in claim 56 (patented claims 17 and 18 recite these agents as the carriers). As also evident from instant specification on page 9, lines 20-22, it would have been obvious to one of ordinary skill in the art that instant generic 'insulin' could be in the form of an 'amorphous' powder as claimed in the patent.

3. Claims 15-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-26 of U.S. Patent No. 6,582,728. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Instant claims 20-24 are drawn to insulin compositions for pulmonary delivery (powder) in insulin amounts between 5 to 99 % and containing citrate or raffinose, trehalose or mannitol with sizes below 10 micrometers. The patented claim is a product by process claim and drawn to a powder composition containing a pharmaceutically active macromolecule and a pharmaceutically active carrier which is a salt or a carbohydrate. Instant claims 15-19 are drawn to a method of preparing insulin powder by spray drying. The patented claims are drawn to a spray drying process for pharmaceutically active molecules and recite specific spray drying conditions. Patented claims thus are generic with respect to active agent and instant claims are generic with respect to the spray drying process. As evident from example 1 in the patent, insulin is one of the intended macromolecule; the specification on col. 7 also indicates that raffinose, trehalose, mannitol (carbohydrates and sodium citrate (salt) are the carriers and the insulin powder is prepared by spray drying process. The patented dependent claim 10 recites the particle sizes of less than

10 micrometers. Instant claims therefore, fall within the scope of the patented claims with regard to claimed insulin and claims thus are anticipated by the patented claims.

4. Claims 20-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28-41, 43-49 and 51-57 of copending Application No. 10/141,044. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both copending application and instant application are drawn to the same insulin powder composition with overlapping amount ranges (instant amounts are 5 to 99% as opposed to 15 to 80 % in the copending application). The specific size ranges for insulin particles in instant claims are deemed to be included in the independent claim 26 of the copending application, which is generic with regard to the size ranges. Similar is the case with regard to instant claim 20 which is generic with respect to the pharmaceutical carrier and instant citrate in claim 26, trehalose in claim 49, mannitol in claim 55, raffinose in claim 56 of the copending application (instant claims 22 and 23 recite these agents as the carriers).

5. Claims 1-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-20 of U.S. Patent No. 5,775,320. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Both instant claims and patented claims are drawn to a method of producing an aerosolized medicament involving the same steps. The patented claims are generic with regard to instant claimed 'insulin' and instant claims are generic with regard to the dose of the

medicament (aerosolized dose from 10 ml to 750 ml). Instant insulin falls within the scope of 'medicament' in the patented claims and therefore, patented claims anticipated instant insulin. With regard to instant claims, which are generic with respect to the dosage, it is deemed obvious to one of ordinary skill in the art to vary the dosages since this amount depends on the severity of the condition and the size of the patient.

6. Claims 1-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,458,135. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Both instant claims and patented claims are drawn to a method of producing an aerosolized medicament involving the same steps. The patented claims are generic with regard to instant claimed 'insulin' and instant claims are generic with regard to the dose of the medicament (aerosolized dose from 10 ml to 750 ml). Instant insulin falls within the scope of 'medicament' in the patented claims and therefore, patented claims anticipated instant insulin. With regard to instant claims, which are generic with respect to the dosage, it is deemed obvious to one of ordinary skill in the art to vary the dosages since this amount depends on the severity of the condition and the size of the patient.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 8 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 360 340.

EP teaches a method of nasal administration of insulin powders containing lactose. The amount of insulin falls within the range recited in instant claims (abstract, col. 6, line 1, Examples and claims).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-14 and 20-22 and 24-25 are rejected under 35 U.S.C. § 103 as being unpatentable over WO 93/00951 by itself or in combination with Rubsamen (5,364,838) or vice versa.

WO discloses essentially the same method for the delivery of any medicament. The method is particularly useful for protein active agents and further contains a carbohydrate, mannitol. The particle sizes are 1-5 micrometers. According to WO the method of delivery using this method is accurate and solves the problems associated

with the delivery of therapeutic proteins and polypeptides by inhalation (note the abstract, page 3, line 28 through page 4, line 10, page 8, lines 5-19, Experimental on pages 18-19 and claims). According to page 19, lines 34-38 of WO, a solution of a protein (albumin) and mannitol is spray-dried and used in the inhalation device.

What is lacking in WO is the teaching that the protein active agent is insulin and the preparation of a spray-dried insulin. However, in view of WO's teachings that the method is applicable for the aerosol delivery of generic 'proteins', it would have been obvious to one of ordinary skill in the art to practice the method with spray-dried insulin as the medicament with a reasonable expectation of success. Instant invention thus, an obvious extension of the teachings of WO.

An artisan would be further motivated to use insulin in the generic 'proteins' of WO since the reference of Rubsamen shows the routine practice in the art of administering insulin in powdery formulations using an aerosol apparatus (note the abstract). Although Rubsamen does not teach carbohydrates, he teaches the use of a 'suitable pharmaceutical carrier' along with insulin (col. 14, lines 42-45) and thus, the use of art known carriers such as lactose while administering small amounts of insulin is within the skill of the art. Since the amount of insulin depends upon the severity of the disease state and the size of the patient as also recognized by Rubsamen on col. 8, lines 29-31, it is deemed to be a manipulatable parameter. The criticality of the product produced by spray drying as in claim 24 is not readily apparent to the examiner. Since this is a product claim, and since both WO and Rubsamen teach dry powder product, it

is deemed obvious to one of ordinary skill in the art to use a suitable drying method as long as it preserves the biological activity of insulin.

Alternately, the use of the method of aerosol delivery of protein drugs taught by WO for insulin taught by Rubsamen would have been obvious to one of ordinary skill in the art because of the advantages taught by WO.

11. Claims 15-25 are rejected under 35 U.S.C. § 103 as being unpatentable over WO 93/00951 by itself or in combination with Rubsamen (5,364,838) or vice versa as set forth above, further in view of Chien (5,042,975), or Markussen (4,946,828) or JP 56 138 110.

The teachings of WO and Rubsamen been discussed above. These references do not teach the use of buffers, particularly citrate as the buffer for insulin. Such a use however, would have been obvious to one of ordinary skill in the art since Chien, Markussen, each teach that these salts are commonly used in combination with insulin and an artisan would expect similar results (note the examples14 and 15 in Chien; Example 7 in Markussen). One of ordinary skill in the art would be motivated further to use citrate buffers in insulin preparations since JP 56 138 110 teaches that the mucosal absorption of insulin is improved by this buffer (note the abstract).

12. Claims 15-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Platz (5,354,562) in view of Chien (5,042,975), or Markussen (4,946,828) or JP 56 138 110, further in view of Maniar (5,482,927), Okada (4,211,769), Hirai (4,659,696). Platz teaches a method of preparation of insulin by dissolving in an appropriate aqueous medium and freeze-drying the solution to obtain insulin powder. Platz further

teaches the addition of various stabilizers such as mannitol, lactose and trehalose (note the abstract, columns 3-4, examples and claims). Platz does not teach the use of citrate as the buffer for insulin. Such a use however, would have been obvious to one of ordinary skill in the art since Chien; Markussen each teaches that these salts are commonly used in combination with insulin and an artisan would expect similar results (note the examples14 and 15 in Chien; Example 7 in Markussen). One of ordinary skill in the art would be motivated further to use citrate buffers in insulin preparations since JP 56 138 110 teaches that the mucosal absorption of insulin is improved by this buffer (note the abstract). Platz also does not teach that the insulin solution be spray dried to obtain the powder form of insulin. The references of Maniar (5,482,927), Okada (4,211,769), Hirai (4,659,696) each teach that powders of biologically active proteins can be obtained from solutions either by freeze-drying or spray drying. (Note col. 3, line 50 et seq. of Maniar; col. 5, line 10 et seq. Of Hirai; col. 4, line 62 et seq.,of Okada). Spray drying the insulin solutions to prepare powders instead of lyophilization taught by Platz or EP would have been obvious to an artisan since the references of Okada, Maniar and Hirai show that protein solutions can either be spray dried or lyophilized to obtain powders. An artisan would be motivated to use either of these methods as long as the powders obtained are still biologically active. The use of appropriate buffer salts such as citrate or acetate for use with insulin is deemed to be within the skill of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK